REMARKS

Reconsideration of the rejection of all claims is respectfully requested in view of the following amendments and arguments. Claims 1-24 were initially filed with this application, and are noted as pending in the Office Action Summary. However, in the Double Patenting rejection beginning at page 6, claims 1-12, 18, 26 and 27 have been provisionally rejected. It is presumed that this was a clerical error, inasmuch as the remainder of the Action deals only with claims 1-24.

Each of claims 1-24 has been either amended or canceled in a manner that is believed to address and overcome or obviate each ground for rejection set forth in the Action.

Specification Amendments

The Title of the Invention has been amended from that shown on published PCT Application WO 03/091232 A2 to the more complete title shown on published PCT Application WO 03/091232 A3, the former having been used by the US PTO and the latter having been used in the Declaration, Assignment and all other papers filed by Applicants herein. The above amendment formally updates the Title.

The "371 status" of this application has been inserted as the first sentence, as requested by the Examiner.

Claim Amendments

In summary of the claim amendments, claims 3-8 and 11 have been amended to change their dependency to recite claim 1 only, so as to avoid improper multiple dependency of the composition claim, which is dependent on any one of claims 1 to 10. Additionally, all claims have been amended (where needed) to remove the unnecessary reference to "solvate, solvate of such a salt" and to replace the term "or prodrug" with the more specific "or *in vivo* hydrolysable ester or amide formed on an available carboxy or hydroxy group." This will be discussed further below in context of the 35 USC 112, first paragraph, claim rejections. Also, many of the claims have been reformatted to more distinctly set off the definitions of the various moieties by use of hanging indents. Additionally and more specifically:

- Claim 1 has been amended to add near the end thereof separate definitions for each of the terms:

- "heteroaryl," specification support therefore been found at page 10, line 17-19;
- "heterocyclyl," specification support therefore been found at page 10, line 31-page 11, line 2; and
- "carbocyclyl," specification support therefore being found at page 11, lines 17-19.

- Claim 8, the two recitations of "as depicted above" have been clarified to read "as depicted in claim 1."
- Claim 9, the recitation of "as depicted in claim 1" has been changed to "as claimed in claim 1."
- Claim 10, the reference to "of formula **(I)**" has been deleted as unnecessary and confusing inasmuch as each listed compound named is complete without reference to the formula, and the structure of formula **(I)** and does not appear in this independent claim.
- Claim 11, at the end thereof, the subjective recitation of "thereafter if necessary or desirable" has been changed the more object is "thereafter optionally."
- Claims 12-15 has been canceled as being in a "use" format, not generally accepted under US practice.
- Method claim 16 has been cancelled in order to expedite the prosecution of this application, and its cancellation is without waiver or prejudice to Applicants' right to prosecute the subject matter thereof in one or more continuing applications.
- Claims 18-24 have been canceled, without prejudice to applicant's right to pursue the subject matter thereof in one or more divisional applications. In this regard, the Examiner states that "the compositions of claims 18-24 art not so linked as to form a single inventive concept," and that "these compositions are so diverse in scope that prior art anticipating one composition under 35 USC 102 would not render obvious another composition of the same claim under 35 USC 103," which the undersigned understands to be akin to a restriction requirement -- otherwise the reason for this statement is not understood.

No new matter has been added by the above amendments, and therefore entry of these amendments is believed to be in order and is respectfully requested. Following entry of these amendments, claims 1-11 and 17 remain pending in this application.

Priority

The introductory phrase making reference to the 371 status of this application has been inserted as the first sentence of the specification, as requested by the Examiner.

Claim Rejections – 35 USC § 112, 2nd Paragraph

Claims 1-24 have been rejected under 35 USC §112, second paragraph, as being indefinite on several grounds i) through vi). It is believed that each of these grounds has been overcome by the above amendments as follows:

i) The asserted indefiniteness of the term "heteroaryl" has been overcome by the insertion at the end of claim 1 a definition of this term taken from the specification at page 10, line 17-19.

ii) The asserted indefiniteness of the term "heterocyclyl" has been overcome by the insertion at the end of claim 1 a definition of this term taken from the specification at page 10, line 31-page 11, line 2.

iii) The asserted indefiniteness of the term "carbocyclyl" has been overcome by the insertion at the end of claim 1 a definition of this term taken from the specification at page 11, lines 17-19.

iv) the Examiner asserts that it is unclear what the "prodrug" looks like. The Examiner's attention is respectfully called to the specification at page 12, line 32 through page 13, line 24, where the term "prodrug" is discussed and exemplified. However, in order to accelerate the examination and allowance of this application, the term "prodrug" has been replaced throughout the claims with the more specific phrase "or *in vivo* hydrolysable ester or amide formed on an available carboxy or hydroxy group," as it is described in the above-referenced portion of the specification. A number of examples of suitable esters formed on an available carboxy or hydroxy group, and of suitable amides formed on available carboxy groups, are also given by way of example in the above-referenced portion of the specification. It is respectfully

submitted that the specification description and exemplification of prodrugs in the form of an *in vivo* hydrolysable ester or amide formed on an available carboxy or hydroxy group provides ample guidance to the persons skilled in this art to identify and use appropriate esters and amides as now claimed, thereby overcoming this ground for rejection.

v) The rejection of claim 9 as not being a proper independent claim, and the rejection of claim 10 with respect to the improper reference to formula (I) in an independent claim, have been overcome by the above amendments to the claims 9 and 10.

vi) The Examiner's concern with claims 18-24 as including additional ingredients "which are not known" has been obviated by the cancellation of these claims.

Claim Rejections – Improper "Use" Format

The objection to claims 12 and 13 as being "substantial duplicates" of claim 1 (by reason of their being in a "use" format) has been obviated by the cancellation of these claims. The rejection of claims 14 and 15 under 35 USC §101 (and also as being indefinite by reason of their being in a "use" format) has also been obviated by the cancellation of these claims.

Claim Rejections – 35 USC § 112, 1st Paragraph

Claims to 1-24 have been rejected under 35 USC §112, first paragraph, the Examiner noting that the specification, while being enabling for a pharmaceutical salt, does not reasonably provide enablement for solvates or solvates of the salts of the compound of formula (I).

Applicants do not agree with this ground for rejection. Nevertheless, as an expediency and in the interest of advancing the prosecution of this application to allowance, Applicants have removed the term "solvate" from all claims. It is Applicants' position that the term "solvate" is already redundant and its removal does not affect the scope of these claims. In particular, Applicants maintain that any person skilled in this art would clearly be aware of what a solvate is, and that this art is sufficiently developed so that such skilled persons would have no difficulty in determining what solvent components of a solvate would be acceptable within the context of the claimed compounds and compositions. Nevertheless, it is apparent that whether a chemically defined compound is or is not in the form of a solvate is

immaterial to the scope of these claims, and this superfluous recitation has therefore been removed by the above amendments, thus obviating this ground for rejection.

A solvate, in the pharmaceutical context as defined in Stedman's Medical Dictionary (and similarly in the PDR Medical Dictionary), is simply "a nonaqueous solution or dispersoid in which there is a noncovalent or easily reversible combination between solvent and solute, or dispersion means and disperse phase; when water is the solvent or dispersion medium, it is called a hydrate." The solvent molecule of a solvate has been described as a species introduced into the crystal and no part of the organic host molecule is left out or replaced (see, *e.g.*, West, Solid State Chemistry at page 358). Thus, whether a chemically defined compound is or is not noncovalently associated with a solvent does not affect the scope of the claim to the compound, *per se*, any more than placing such compound in solution would remove the compound from the scope of such claim. Therefore, the alternative recitation of "a solvate ... thereof" is seen as being entirely superfluous, and neither expands nor contracts the scope of these claims. In other words, a claim to a novel compound *per se* encompasses such compound, regardless of its state of solvation or hydration, or its polymorphic form, and regardless of whether it is a racemic mixture or a resolved enantiomer.

Therefore, since the alternative recitation of "a solvate ... thereof" does not, and is not intended to, expand or limit the scope of these claims, all reference to the compounds alternatively being in the form of a "solvate" has been removed from the claims in order to expedite the prosecution of this application to allowance. This ground for rejection has therefore been overcome by the cancellation of this term from all claims.

Claim 24 has been separately rejected under 35 USC §112, first paragraph, as failing to comply with the enablement requirement, beginning at the bottom of page 4 of the Action. As noted above, claim 24 has been canceled by the above amendments and, therefore, this ground for rejection has been obviated.

Double Patenting

Claims 1-12, 18, 26 and 27 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims of copending Application No. 10/488,870 (as noted above, there is no claim 26 or claim 27, so it is not clear what claims the Examiner is intending to refer to). The Examiner asserts that although the conflicting claims are not identical, they are not patentably distinct from each other because the claimed subject matters overlap the scope, *i.e.*, it is asserted that the copending application teaches a generic group of compounds which embraces Applicants' claimed compounds. This ground for rejection is respectfully traversed.

First of all, the Examiner is advised that Application No. 10/488,870 has now issued as US Patent 7,132,416 on November 7, 2006, and therefore this rejection is no longer provisional. While Applicants do not necessarily agree with this ground for rejection, in order to expedite the prosecution of this application to allowance, a Terminal Disclaimer is being filed herewith relative to US Patent 7,132,416. However, this Terminal Disclaimer is being submitted with the understanding that the filing of this Terminal Disclaimer is not intended to be, and does not constitute, an admission that an obviousness-type double patenting rejection would be proper between the claims of this reference and the presently claimed invention (*see* MPEP 804.02 II).

Examiner's Comment on Published PCT Applications

At page 7 of the Action, the Examiner comments:

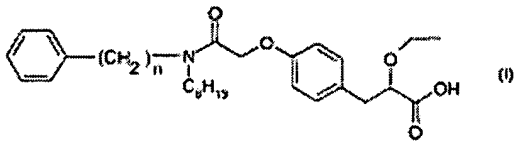
> During the search, the documents WO 2003/051821 and WO 2003/051822 were found which have copending corresponding U.S. applications. Applicants are urgently requested to make these of record and point to the line of demarcation between all of these applications.

The reason for this comment was not initially understood in that both of these published applications relate to substituted phenylpropionic acid derivatives as agonists to human peroxisome proliferator-activated receptor alpha (PPAR), and not to the benzothiadiazapine derivatives of the present invention, having an IBAT inhibitory effect. However, on further investigation (the undersigned is not an attorney on the US applications corresponding to the

cited PCT applications) it was noted that certain claims were directed toward a combination of such phenylpropionic acid derivatives with an IBAT inhibitor. Although original claims 23 and 24 of the present application were directed toward a pharmaceutical composition comprising a combination of the presently claimed benzothiadiazapine derivatives together with a PPAR alpha and/or gamma agonist, claims 23 and 24 have been cancelled as noted above. Moreover, it is understood by the undersigned that the specific PPAR agonist recited in original (now cancelled) claim 24 is disclosed in WO 99/62872, which is cited on page 46 of the present specification. Therefore, the claims of the U.S. National Stage applications corresponding to WO 2003/051821 or WO 2003/051822 are not believed to be relevant to the presently claimed invention.

Nevertheless, in compliance with the Examiner's request and for the sake of making a complete response, the following is noted:

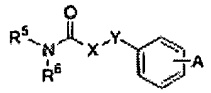
- **WO 2003/051821** is International Application PCT/GB02/05738 filed December 18, 2002 and published on June 26, 2003, and is directed toward substituted phenylpropionic acid derivatives as agonists to human peroxisome proliferator-activated receptor alpha (PPAR) of the general structure of formula (I):



(I)

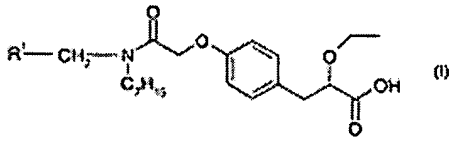
This PCT application entered the U.S. National Stage on June 18, 2004 as U.S. Application No. 10/499,378, with a 371(c) date of March 4, 2005, and published as US 20050171204 A. The status of this application is currently listed in PAIR as "Docketed New Case - Ready for Examination." It is understood from PAIR (the undersigned is not the attorney on this application) that all currently pending claims are directed toward the S enantiomer of a compound of the above formula (I) and pharmaceutically acceptable salts, solvates, crystalline forms and prodrugs thereof. It is noted, however, that claims 18 and 19 currently pending in that application are directed toward a combination of a composition of formula (I) with an IBAT inhibitor (claim 19 including a list of various specific IBAT inhibitors).

Pending Application No. 11/026,806 was filed on December 12, 2004 as a continuation-in-part of Application No. 10/499,261, and was published as US 20050282022, and is directed toward the S-enantiomer of the compound of formula I:



most particularly to benzenepropanoic acid derivatives. It is understood from PAIR (the undersigned is not the attorney on this application) that all claims currently pending in that application are directed toward compounds of the above formula (I), and no pending claim is directed toward such compound in combination with an IBAT inhibitor. A non-final rejection was mailed on October 2, 2006.

- **WO 2003/051822** is International Application PCT/GB02/05744 filed December 18, 2002 and published on June 26, 2003, and is directed toward substituted phenylpropionic acid derivatives as agonists to human peroxisome proliferator-activated receptor alpha (PPAR) of the general structure of formula (I):



This PCT application entered the U.S. National Stage on September 7, 2004 as U.S. Application No. 10/499,378 and published as 20050113362 A. The status of this application is currently listed in PAIR as "Final Rejection Mailed [mailed October 5, 2006]." It is understood from PAIR (the undersigned is not the attorney on this application) that all claims currently pending in that application are directed toward compounds of the above formula (I) and pharmaceutically acceptable salts, prodrugs or various esters thereof. It is noted, however, that claims 18, 19 and 22 currently pending in that application are directed toward a combination of a composition of formula (I) with an IBAT inhibitor (claims 19 and 22 including an list of various specific IBAT inhibitors). Claims 18 and 19 stand rejected, and claim 22 has been indicated as allowed.

Neither WO 2003/051821 nor WO 2003/051822 is prior art with respect to the present application, and inasmuch as no claim now pending in the present application is directed toward or includes any reference to a PPAR agonist, this factor alone provides a clear line of demarcation of the present claims from the perspective of obviousness-type double patenting relative to the above-identified pending U.S. applications.

Conclusion

All grounds for rejection and/or objection having been address and overcome by the above amendments and/or arguments, it is believed that all pending claims are in condition for allowance, and a Notice to that effect is believed to be in order and is respectfully requested.

Except for issue fees payable under 37 C.F.R. §1.18, the Director is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account No. 50-0310. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. §1.136(a)(3).

Respectfully Submitted,
Morgan Lewis & Bockius LLP

Date: January 10, 2007 By: _____

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